[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Highly Potent and Selective Deubiquitinating Enzyme Inhibitor

Description of Technology: Available for licensing are inhibitors that target the USP1/ UAF1 deubiquitnating enzyme (DUB) complex. The FDA approval and commercial success of Velcade®, a small molecule proteasome inhibitor, has established the ubiquitin-proteasome system (UPS) as a valid target for anticancer treatment. However, proteasome inhibitors in general suffer from a narrow therapeutic index and acquired resistance. A promising alternative to proteasome inhibition has been to target the enzymes upstream of proteasome-mediated protein degradation, i.e. the ubiquitin conjugation and deconjugation, to generate more specific, less toxic therapeutic agents. The investigators have developed small molecules that target the USP1/ UAF1 DUB complex that acts upstream of UPS and has been implicated in the DNA damage response. These compounds are the most potent and selective DUB inhibitors reported to date. Moreover, the inhibitors act synergistically with cisplatin, a DNA damaging anti-cancer drug, to overcome chemoresistance and enhance cytotoxicity. These results suggest the inhibitors may also improve the efficacy and potency of other commonly prescribed chemotherapeutic agents that are known to induce DNA damage.

Potential Commercial Applications:

• Method to treat cancer

• Method to overcome chemoresistance to cisplatin

• Pharmaceutical compositions

Competitive Advantages:

• Represents the most potent and selective DUB inhibitor reported to date.

• Promising alternative to proteasome inhibition offering the potential of more selective and less toxic therapeutic agents.

• Acts synergistically with DNA damaging agents to overcome chemoresistance.

Development Stage:

• Early-stage

• In vitro data available

Inventors: David Maloney (NCATS), Andrew Rosenthal (NCATS), Ajit Jadhav (NCATS), Thomas Dexheimer (NCATS), Anton Simeonov (NCATS), Zhihao Zhuang (University of Delaware), Qin Liang (University of Delaware), Diane Luci (NCATS)

Intellectual Property: HHS Reference No. E-043-2013/0 – US Provisional Application No. 61/747,052 filed 28 December 2012

Related Technologies:

• HHS Reference No. E-208-2007/0 – US Patent Application No. 12/669,361 filed 15 January 2010

• HHS Reference No. E-156-2012/0 – US Provisional Application No. 61/692,560 filed 23 August 2012

• HHS Reference No. E-231-2002/0 – US Patent No. 7,498,336 issued 3 March 2009

• HHS Reference No. E-070-2005/0 – US Patent No. 8,242,160 issued 14 June 2012 and US Patent Application No. 13/547,417 filed 12 July 2012

Licensing Contact: Jennifer Wong, M.S.; 301-435-4633; wongje@mail.nih.gov

Collaborative Research Opportunity: The National Center for Advancing Translational Sciences is seeking statements of capability or interest from parties

interested in collaborative research to further develop, evaluate or commercialize this invention. For collaboration opportunities, please contact Lili Portilla at lili.portilla@nih.gov.

Therapeutic Applications of a Carboxy-Terminal RTDL Motif

Description of Technology: Mesencephalic Astrocyte-derived Neurotrophic Factor (MANF) is a secreted neurotrophic factor with known anti-neurodegenerative properties. The inventors discovered that the C-terminal RTDL motif of MANF is involved in the anti-degenerative properties of MANF and association of extracellular MANF with the cell surface. Isolated peptides, including the C-terminal RTDL motif of MANF, potentially can be used as a treatment for neurodegenerative disorders and ischemia.

Potential Commercial Applications: Treating neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, Huntington disease, etc.

Competitive Advantages: Secreted novel peptides.

Development Stage:

- Early-stage
- Pre-clinical
- In vitro data available

Inventors: Brandon K Harvey, et al. (NIDA)

Intellectual Property: HHS Reference No. E-249-2012/0 – US Provisional Application 61/732, 241 filed 30 Nov 2012

Licensing Contact: Betty B. Tong, Ph.D.; 301-594-6565; tongb@mail.nih.gov

HIV-Neutralizing Polypeptides: A Novel Use for Platelet Factor 4 or Its Derivatives

Description of Technology: The subject invention describes the method for using Platelet Factor 4 (PF4), also called CXCL4, to inhibit HIV viral entry by blocking GP120 independent of HIV receptor. It also demonstrates that the active polypeptide fragment(s) of PF-4 could be used to identify potential peptide mimics or small molecules that could be used to inhibit HIV infection. PF4 and/or its derivatives may be developed as a systemic therapy or preventive measure using topical applications, such as microbicides. In addition, CXCL4 serum/plasma testing could be used as a clinical marker of HIV disease status to predict/monitor the efficacy of treatment and determine the prognosis of a subject with HIV infection.

Potential Commercial Applications:

• Treatment and prevention of HIV-1 infection.

• Topical application as microbicides.

• A vaccine adjuvant to boost the vaccine efficacy.

• A clinical marker of HIV disease status or to predict/monitor the efficacy of treatment or vaccines.

Competitive Advantages:

• A new HIV-1 inhibitory molecule that acts through a new inhibitory mechanism.

• Any potential derivative or mimicking compound would be unique and have the advantage of hitting a previously unrecognized molecular target in the HIV life cycle.

Development Stage:

• Early-stage

• In vitro data available

Inventors: Paolo Lusso and David J. Auerbach (NIAID)

Publication: Auerbach DJ, et al. Identification of the platelet-derived chemokine CXCL4/PF-4 as a broad-spectrum HIV-1 inhibitor. Proc Natl Acad Sci USA 2012 Jun 12;109(24):9569-74. [PMID 22645343]

Intellectual Property: HHS Reference No. E-140-2012/0 – US Application No. 61/649,150 filed 19 Jun 2012

Related Technology: The CXCL4 sequence is in the public domain.

Licensing Contact: Sally Hu, Ph.D., MBA; 301-435-5606; hus@mail.nih.gov

Polarimetric Accessory for Colposcope

Description of Technology: Available for licensing and commercial development is a colposcope accessory device that compensates and resolves tissue borne specular reflections. In medical diagnostic procedures for examining the cervix and the tissues of the vagina and vulva, long working-distance (-30 cm) lighted binocular microscope (colposcope) that provide up to 25x optical magnification are used to create an illuminated magnified view. Speculum dilations can give rise to specular reflections from the tissue surface. The present polarimetric accessory overcomes this limitation and enhances the visibility of subsurface structures of the scattering object. Linearly polarized light is used for cervical illumination and imaging is performed through an additional polarizer that separates the specularly reflected light from the diffusely backscattered light, which originates in deeper tissue layers, allowing enhanced imaging of the hidden subsurface tissue structure (texture). The region of interest is illuminated by linearly

polarized light, and backscattered light passes through the polarization filter to be detected by a digital camera. A custom optical design preserves the polarization state of the backscattered light in the microscope, without interfering with the standard optical path and operation of the microscope, including its binocular system. Special algorithms to visualize regions of statistical similarity in the image have been developed. Though the diffusely backscattered light presents only a small fraction of the detected light, its analysis, using the customized design and image processing procedures, provides useful information about internal structures of biological tissues. The polarimetric accessory includes a linear polarizer for the illuminating beam, two beam splitters for preserving polarization state, lens system for imaging, polarization analyzer, band-pass optical filter, digital camera, and electronic triggering system.

Potential Commercial Applications: Gynecological examinations

Competitive Advantages:

• Image quality

• Resolution of tissue structures at close microscopic distances

Development Stage: Prototype

Inventors: Amir Gandjbakhche (NICHD), Victor Chernomordik (NICHD), Moinuddin Hassan (NICHD), Alexander Sviridov (NICHD), Zachary Alissi (NICHD), Paul Smith (NIBIB), Albert Boccara (NICHD)

Publications:

1. Jacques SL, et al. Imaging superficial tissues with polarized light. Lasers Surg Med. 2000;26(2):119-29. [PMID 10685085]

2. Jacques SL, et al. Imaging skin pathology with polarized light. J Biomed Opt. 2002 Jul;7(3):329-40. [PMID 12175282]

3. Ramella-Roman JC, et al. Design, testing, and clinical studies of a handheld polarized light camera. J Biomed Opt. 2004 Nov-Dec;9(6):1305-10. [PMID 15568952]

4. Sviridov AP, et al. "Analysis of Biological Tissue Textures Using Measurements of Backscattered Polarized Light" (presented at the Optical Society of America - Biomedical Optics Topical Meeting, Fort Lauderdale, Florida, March 2006).

5. Sviridov AP, et al. Visualization of biological texture using correlation coefficient images. J Biomed Opt. 2006 Nov-Dec;11(6):060504. [PMID 17212522]

Intellectual Property: HHS Reference No. E-084-2012 – US Provisional Patent Application No. 61/620,295 filed 04 Apr 2012

Licensing Contact: Michael A. Shmilovich, Esq., CLP; 301-435-5019; shmilovm@mail.nih.gov

CpG Oligonucleotides Treatment to Prevent Chemotherapy-Induced Pulmonary Toxicity

Description of Technology: Bleomycin (BLM) is a chemotherapy agent used to treat multiple types of cancer, but its side effects are life threatening for some patients. About 20% of patients undergoing BLM chemotherapy develop interstitial pneumonitis which may develop to life threatening fibrosis. In such cases, BLM chemotherapy cannot be continued.

This invention identifies a method of pre-treatment using immunostimulatory CpG Oligonucleotide (ODN) molecules to prevent chemotherapy-induced pulmonary

toxicity. Administration of certain ODN molecules induces inflammation via stimulation of inflammatory genes (Toll-like receptor 9/TLR9). This stimulation is subsequently down-regulated. This technology makes use of this counter regulatory mechanism to reduce the side effects of chemotherapy agents, such as BML. A properly timed pre-administration of ODN molecules, prior to BML therapy, prevents the lethal side effect of BLM-induced pulmonary inflammation and down-regulates promoters of BLM toxicity (IL-17A and TGF-beta1). Because toxicity from pulmonary inflammation is a side effect limiting use of many chemotherapeutic agents and ODN molecules are relatively inexpensive and have a favorable safety profile, this technology may be useful to improve treatment protocols for many chemotherapy agents.

Potential Commercial Applications: Therapeutic to reduce harmful side effects of pulmonary inflammation caused by chemotherapy.

Competitive Advantages:

• Pulmonary toxicity during chemotherapy is dangerous side effect, this technology uses ODN molecules that are relatively inexpensive and have a favorable safety profile to reduce this side effect.

• This technology may increase the safety and availability of many chemotherapy treatments.

Development Stage:

• Early-stage

• In vivo data available (animal)

Inventors: Dennis Klinman and Takeshi Kinjo (NCI)

Publication: Kinjo T, et al. The counter regulatory response induced by CpG oligonucleotides prevents bleomycin induced pneumopathy. Respir Res. 2012 Jun 18;13:47. [PMID 22708497]

Intellectual Property: HHS Reference No. E-077-2012/0 – U.S. Provisional Patent Application No. 61/643,088 filed 04 May 2012

Licensing Contact: Edward (Tedd) Fenn; 301-435-5031; fenned@mail.nih.gov

Collaborative Research Opportunity: The National Cancer Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize CpG oligonucleotides for use to down-modulate inflammatory reactions. For collaboration opportunities, please contact John D. Hewes, Ph.D. at hewesj@mail.nih.gov.

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Date

Richard U. Rodriguez,
Director
Division of Technology Development and Transfer
Office of Technology Transfer
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